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STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| HAQ, SHAFIQUL | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,094 | SAINI ET AL. | |
| | Examiner | Art Unit | |
| | SHAFIQUL HAQ | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of claims*

1. Claim 1, 3-7 and 9-11 are pending and are examined on merits.

### *Claim Objections*

2. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The method of claim 1 generates monoclonal antibody capable of binding to methyl tert-butyl ether ("MTBE") (see line 9), however, claim 7 antibodies as claimed is binds to methyl tert-butyl ether, ethyl tert-butyl ether, methyl tert-amyl ether and ter-butyl alcohol and thus claim 7 failed to further limit claim 1.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3-7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 2 defines “X is a spacer” in line 4. The term “spacer” is not defined or described in the specification and thus it is unclear what compounds other than 5 carbon alkylene are encompassed by the term “spacer”. Specification disclose

MTBE-spacer-BSA polymer as 7-methoxy-3,7-dimethyloctanal-BSA (see example 1, page 19 of specification) which would provide 5 carbon alkylene chain as a spacer but specification does not disclose or describe any other compound that could be used as a spacer. Therefore, is it unclear what other compounds are encompassed by the term "spacer" in claim 1.

6. Claim 1 defines “B as a group capable of binding to a carrier protein” in line 4. The term “group capable of binding to a carrier protein” is not defined or described in the specification and thus it is unclear what groups are encompassed by the term “group capable of binding to a carrier protein”. Specification discloses MTBE-spacer-BSA polymer as 7-methoxy-3,7-dimethyloctanal-BSA (see example 1, page 19 of specification) which contains a aldehyde group but specification does not disclose or suggest any other group usable together with the compound for binding to a carrier protein. Therefore, is it unclear what other group applicants is intended to encompass by the term "group capable of binding to a carrier protein" in claim 1.
7. With regard to claim 9, the claim recites “a method for assaying a sample for fuel oxygenate". It is unclear the assay/immunoassay is intended for what? Detection of fuel oxygenates? Quantitation of fuel oxygenates? Binding assay? Further, the claim provides for assaying a sample using the antibodies generated by the method according to claim 1 by immunoassay, however, the claim is incomplete for not reciting any immunoassay steps and for not clearly defining how is the immunoassay is correlated to the assaying of the sample.

8. Claim 9 recites “fuel oxygenates and their breakdown products" in lines 1-2. The “breakdown products” of fuel oxygenates are not clearly defined in the specification and thus it is not clear what compounds are encompassed by the term “breakdown product” useful for assaying that would be recognizable by the antibody produced by the method of claim 1.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating antibody capable of binding to methyl tert-butyl ether (MTBE), ethyl tert-butyl ether (ETBE), methyl tert-amyl ether (TAME) and tert-butyl alcohol (TBA), does not reasonably provide enablement for generating antibody capable of binding to all fuel oxygenates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The term “Fuel oxygenates” is not clearly defined in the specification, however the term includes any oxygen-containing compounds (i.e. oxygenates) that have been added to any "fuel" (i.e. a flammable substance). However, if only gasoline is intended for “Fuel”, oxygenates that are commonly added includes methyl tert-butyl ether (MTBE), ethyl tert-butyl ether (ETBE), methyl tert-amyl ether (TAME), tert-butyl alcohol (TBA), di-isopropyl ether (DIPE), tert-amyl ethyl ether (TAEE), tert-amyl

alcohol (TAA), ethanol, methanol and acetone. Since the antibody is generated by using an immunogen comprising methyl tert-butyl group conjugated to a carrier through a spacer, the antibody are expected to only bind to very closely related structures of methyl tert-butyl group (such as MTBE, ETBE, TBA) but not to structurally different groups such as ethanol, methanol, acetone and DIPE that are encompassed by the scope of the term "Fuel oxygenates". In fact, specification of instant application discloses that the antibodies raised against the immunogen recognize MTBE, TAME, TBF and TBA but not the methanol (line 23, page 25 to line2, page 24). Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

11. Claims 1, 3-7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject mater later claimed. The MPEP lists factors that can be used to determined if sufficient evidence of possession has been furnished in the disclosure of the application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or

coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." See MPEP § 2163.

The claims lack adequate written description for the following reasons:

Claim 1 is directed to a method of generating antibodies useful for assaying a sample for fuel oxygenates using immunogen wherein the immunogen comprises a hapten conjugated to a carrier protein and wherein the hapten is CH3O-C(CH3)2-CH2-X-B where X is a spacer and B is a group capable of binding to a carrier protein. The terms "spacer" and “group capable of binding to a carrier” are not defined in the specification. MPEP 2111 states that the broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. In re Cortright, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). Further, MPEP 2111.01 states that the words of a claim must be given their "plain meaning" unless they are defined in the specification. While the claims of issued patents are interpreted in light of the specification, prosecution history, prior art and other claims, this is not the mode of claim interpretation to be applied during examination. During examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, 367 F.3d 1359, 136~), 70 USPQ2d 1827, 1834 (Fed. Cir. 2004). Therefore, the term “spacer” may encompass any linker compounds without regard to any structural features and the term “group” may encompass any functional group. However, the spacer as disclosed in the specification is only limited to a specific compound represented by -CH2CH2CH(CH3)CH2- and "B" is limited to

CHO group. Specification discloses a conjugate 7-methoxy-3,7-dimethyloctanal-BSA as an immunogen for raising antibody against MTBE wherein the spacer reads on -CH2CH2CH(CH3)CH2- (see example 1, page 19 of specification) and "B" reads on CHO, but specification does not disclose or describe any other compound that could be used as a spacer and any other group except CHO that can be used to couple to a carrier. Specification provides no clear guidance as to what other compounds or what structural features would be acceptable as a spacer suitable for linking to a carrier which would generate specific antibody against MTBE. MTBE is a small molecule and small molecule by it self is not immunogenic and a carrier protein must be conjugated to small molecule in order to provoke immuno response and even after conjugating to a carrier protein, the result is not predictable and specification also support this because specification states "this approach is difficult and a very extensive screening program may be required, without guarantee of success" (see specification, lines 6-9 of page 9). Moreover, linking compound (i.e. spacer) and the linkage also influence production of successful antibody against small molecules. A reference (Issert *et al*. Amino Acids 1999) is attached herewith to show that conjugating a carrier to a small molecule (phosalone) through different linkers (spacer) provides different immunogenic response. As for example, the Phosalone compound when conjugated to a carrier through N-carboxypentyl spacer could generate antibody specific to the phosalone but the space N-(2-oxo-3-aza-carboxypentyl) spacer was unable to provide successful antibody production (See Fig. 2 and Fig. 3), which indicates that it is not predictable as to what spacer would

provide a successful production of antibody and that length of linker as well as the linkages (bonds) may be critical to successful production of antibody against small molecules.

Accordingly, it is deemed that the specification fails to provide adequate written description and guidance for linker compounds that could be generated from divergent and undefined structures as encompassed by the term “spacer” and “a group capable of binding to a carrier” suitable for linking to carrier for successful production of antibody that specifically binds to MTBE.

Further, an artisan in the art would not be able to practice the invention because an undue experimentation will be required to judge suitability of “spacer” from structurally divergent linkers/spacers that are encompassed by the term “spacer” in order to provide immunogen to successfully raise antibody that specifically recognizes methyl tert-butyl ether. Undue experimentation will be required to judge suitability of structurally divergent compounds as spacer/linker that that may be encompassed by the term “spacer” with acceptable specificity to methyl tert-butyl ether. Therefore, the instant specification fails to provide sufficient information about the composition and structure of the compounds encompassed by the term "spacer" that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art;

predictability or unpredictability in the art; and breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, the specification fails to provide sufficient support of the broad use of any spacer represented by the term “spacer” and the broad use of any functional group represented by the term "group". As a result, one of skill in the art would be forced to perform an exhaustive search for the embodiments of any “spacer” and any “group” to link to a carrier protein to provide an immunogen as recited in the instant claim suitable to raise antibody capable of specifically binding to methyl tert-butyl ether. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pourfarzaneh (US 6,416,671 B1).

Claim 7 is drawn to a monoclonal antibody according to the method of claim 1 capable of binding to methyl tert-butyl ether (MTBE), ethyl tert-butyl ether, methyl tert-amul ether and tert-butyl alcohol.

Pourfarzaneh discloses MTBE mouse monoclonal antibody capable of binding to MTBE (see example 5 of column 18) but does not mention about binding specificity to other closely related derivative of methyl tert-butyl ether.

However, since the antibody of Pourfarzaneh is capable of binding to MTBE, the antibody is also expected to bind to other closely related derivatives of MTBE and thus the antibody of Pourfarzaneh appears to be the same as or functionally equivalent to the antibodies of instant claim 7 because they have the same specificity i.e. capable of binding methyl tert-butyl ether (MTBE). The phrase “A method according to claim 1” has not given a patentable weight because the patentability of a product (i.e. the antibody) does not depend on its method of production. If the product in the product by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. For product by process claim, see MPEP 2113. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The federal circuit affirmed, stating that "once a product is fully disclosed in the art, future claims to that same product are precluded, even if that product is claimed as made by a new process." Once a product appearing to be substantially identical is found and a 35 USC 102/103 rejection made, the burden shifts to the applicant to show an

unobvious difference. *In re Thorpe* 227 USPQ 964 (Fed. Cir. 1985); *In re Best* 195 USPQ 430 (CCPA 1977); *In re Fessman* 180 USPQ 324 (CCPA 1974); *In re* Brown 173 USPQ 685 (CCPA 1972).

***Response to argument***

14. Applicant's arguments and amendments filed 2/2/09 have been fully considered, and are persuasive to overcome the rejections of 6/24/08 under 35 USC 102/103, 35 USC 101 and some of the rejections under 35 USC 112 second paragraphs. However, Applicants arguments have been rendered moot in view of the new grounds of rejections under 35 USC 112 second paragraph, 35 USC first paragraph and 35 USC 103 as described in this office action necessitated by Applicants amendments and a further review of the claims.

***Conclusion***

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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/Shafiqul Haq/
Examiner, Art Unit 1641